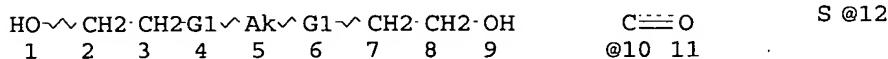


=> d que

L22 1039640 SEA FILE=REGISTRY ABB=ON PLU=ON PMS/CI
L28 STR



VAR G1=10/NH/O/12

NODE ATTRIBUTES:

CONNECT IS E2 RC AT 12

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

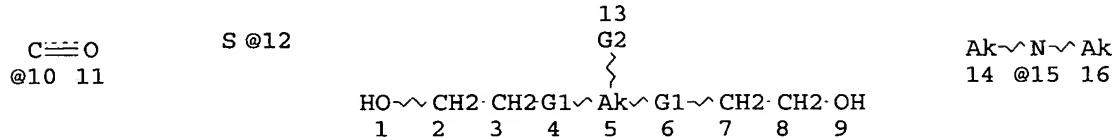
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

L30 4991 SEA FILE=REGISTRY SUB=L22 SSS FUL L28
L31 4979 SEA FILE=REGISTRY ABB=ON PLU=ON L30/COM
L36 STR



VAR G1=10/NH/O/12

VAR G2=X/15

NODE ATTRIBUTES:

CONNECT IS E2 RC AT 12

CONNECT IS E1 RC AT 14

CONNECT IS E1 RC AT 16

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L37 33 SEA FILE=REGISTRY SUB=L31 SSS FUL L36
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=> d l39 ibib abs hitstr 1-5

L39 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:868139 HCAPLUS

DOCUMENT NUMBER: 136:1862

TITLE: Surfactants for herbicidal glyphosate formulations

INVENTOR(S): Lennon, Patrick J.; Chen, Xiangyang; Arhancet, Garciela B.; Glaenzer, Jeanette L.; Gillespie, Jane L.; Graham, Jeffrey A.; Becher, David Z.; Wright, Daniel L.; Agbaje, Henry E.; Xu, Xiaodong C.; Abraham, William; Brinker, Ronald J.; Pallas, Norman R.;

PATENT ASSIGNEE(S): Wideman, Al S.; Mahoney, Martin D.; Henke, Susan L.
 SOURCE: Monsanto Technology, LLC, USA
 PCT Int. Appl., 365 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001089302	A2	20011129	WO 2001-US16550	20010521
WO 2001089302	A3	20030626		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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JP 2003535056	T2	20031125	JP 2001-585556	20010521
BR 2001010978	A	20040113	BR 2001-10978	20010521
US 2002123430	A1	20020905	US 2001-988353	20011119
US 2003087764	A1	20030508	US 2001-988352	20011119
US 2003096708	A1	20030522	US 2001-988340	20011119
WO 2002069718	A2	20020912	WO 2002-US6709	20020301
WO 2002069718	A3	20021031		
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EP 1389912	A2	20040225	EP 2002-713759	20020301
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BR 2002007826	A	20040622	BR 2002-7826	20020301
US 2003104943	A1	20030605	US 2002-926521	20020426
WO 2002096199	A2	20021205	WO 2002-US16032	20020521
WO 2002096199	A3	20031224		
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WO 2002102153	A2	20021227	WO 2002-US15977	20020521
WO 2002102153	A3	20031113		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
NZ 529552	A	20031219	NZ 2002-529552	20020521
EP 1389040	A2	20040218	EP 2002-747849	20020521
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR 2002009919	A	20040824	BR 2002-9919	20020521
BR 2002009940	A	20040824	BR 2002-9940	20020521
PRIORITY APPLN. INFO.:			US 2000-205524P	P 20000519
			US 2000-206628P	P 20000524
			US 2001-273234P	P 20010302
			US 2001-274368P	P 20010308
			WO 2001-US16550	W 20010521
			US 2001-926521	A2 20011114
			US 2001-988340	A 20011119
			US 2001-988352	A 20011119
			US 2001-988353	A 20011119
			WO 2002-US6709	W 20020301
			US 2002-926521	A2 20020426
			WO 2002-US15977	W 20020521
			WO 2002-US16032	W 20020521

OTHER SOURCE(S) : MARPAT 136:1862

AB A herbicidal composition is provided comprising an aqueous solution of glyphosate,

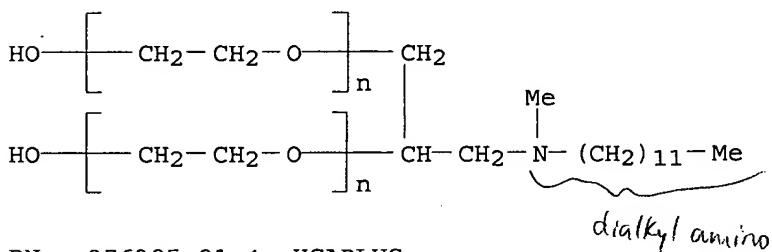
predominantly in the form of the potassium salt, at a concentration ≥ 300 g/L and a surfactant solution or stable suspension, emulsion, or dispersion in the water, at 20-300 g/L, wherein the composition has a viscosity <250 cP at 0° or a Gardner color value <10. The surfactants are amines or quaternary ammonium salts. When the formulation is applied to plants, liquid crystals comprising the surfactant are formed on leaves.

IT 376395-90-3 376395-91-4

RL: MOA (Modifier or additive use); USES (Uses)
(surfactant for herbicidal glyphosate formulations)

RN 376395-90-3 HCAPLUS

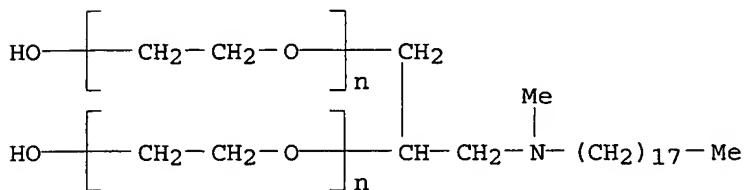
CN Poly(oxy-1,2-ethanediyl), α,α' -[1-[(dodecylmethylamino)methyl]-1,2-ethanediyl]bis[ω -hydroxy- (9CI) (CA INDEX NAME)



RN 376395-91-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α,α' -[1-

[(methyloctadecylamino)methyl]-1,2-ethanediyl]bis[ω -hydroxy- (9CI)
(CA INDEX NAME)



L39 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:101008 HCAPLUS

DOCUMENT NUMBER: 124:260399

TITLE: Preparation of acyl fluoride-containing aliphatic amides

INVENTOR(S): Sato, Shinichi; Koike, Noryuki; Matsuda, Takashi

PATENT ASSIGNEE(S): Shinetsu Chemical Industry Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07316118	A2	19951205	JP 1994-136545	19940526
JP 2966727	B2	19991025		

PRIORITY APPLN. INFO.:

OTHER SOURCE(S): CASREACT 124:260399

AB The amides are prepared by treating acyl fluoride-containing compds. and/or their alcoholates with alkali metal fluorides with silanes having ≥ 1 Si-N bond. N-allylaminotrimethylsilane was treated dropwise with CF₃CF₂CF₂OCF(CF₃)CF₂OCF(CF₃)COF at $\leq 50^\circ$ over 15 min to give 97% CF₃CF₂CF₂OCF(CF₃)CF₂OCF(CF₃)CONHCH₂CH:CH₂.

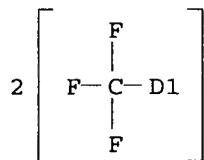
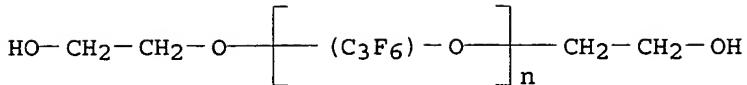
IT 175414-15-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of acyl fluoride-containing aliphatic amides using aminosilanes)

RN 175414-15-0 HCAPLUS

CN Poly[oxy[trifluoro(trifluoromethyl)-1,2-ethanediyl]], α -[trifluoro-2-hydroxy(trifluoromethyl)ethyl]- ω -[trifluoro-2-hydroxy(trifluoromethyl)ethoxy]-, dicesium salt (9CI) (CA INDEX NAME)



6 (D1-F)

●2 Cs

L39 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:485978 HCAPLUS

DOCUMENT NUMBER: 121:85978

TITLE: Water-thinned ink compositions for jet printing

INVENTOR(S): Tabayashi, Isao; Inoe, Sadahiro; Yamada, Yutaka

PATENT ASSIGNEE(S): Dainippon Ink & Chemicals, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06057189	A2	19940301	JP 1992-216879	19920814
PRIORITY APPLN. INFO.:			JP 1992-216879	19920814

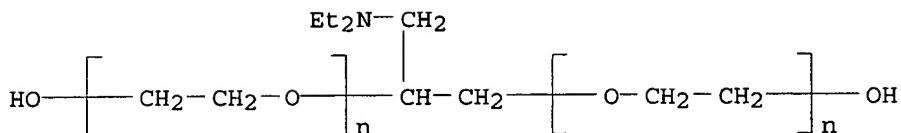
AB The title compns., having pH ≤9.5, good storage stability, and good drying resistance, contain an N-containing functional group-substituted propanediol or its derivs., e.g., 3-diethylamino-1,2-propanediol (I) or ethoxylated (1-6 mol) I, and a carboxylic acid containing ≥1 OH group, e.g., glycolic acid (II), lactic acid, or glyceric acid. A composition (pH 7.0) containing I 1.2, II 1.5, glycerol 8.0, iso-PrOH 3.0, C.I. Food Black 2 3.0, and H2O 83.3 parts contained no precipitate after 6 mo of storage, showed good flowability initially and after 2 wk, and gave good markings on common paper.

IT 156602-91-4

RL: TEM (Technical or engineered material use); USES (Uses)
(jet-printing inks containing, aqueous, storage-stable, drying-resistant)

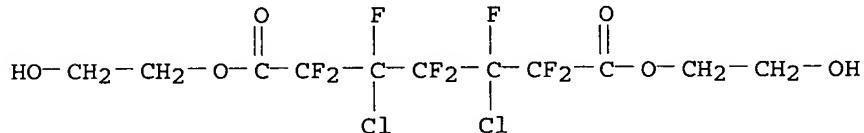
RN 156602-91-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α,α'-[1-[(diethylamino)methyl]-1,2-ethanediyl]bis[ω-hydroxy- (9CI) (CA INDEX NAME)



L39 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1981:157347 HCAPLUS
 DOCUMENT NUMBER: 94:157347
 TITLE: Polyesterification of halogen containing difunctional compounds
 AUTHOR(S): Boutevin, B.; Dongala, E. B.; Pietrasanta, Y.
 CORPORATE SOURCE: Lab. Chim. Appl., Ec. Natl. Super. Chim. Montpellier, Montpellier, Fr.
 SOURCE: Journal of Fluorine Chemistry (1981), 17(2), 113-26
 CODEN: JFLCAR; ISSN: 0022-1139
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The use of acid chlorides easily gives fluorinated and chlorinated polyesters with mol. wts. >3000. A new method of polytransesterification of the bis(hydroxyethyl) esters of fluorinated and chlorinated diacids at <200° is also described.
 IT 77363-24-7P 77363-26-9P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 77363-24-7 HCAPLUS
 CN Heptanedioic acid, 3,5-dichloro-2,2,3,4,4,5,6,6-octafluoro-, bis(2-hydroxyethyl) ester, homopolymer (9CI) (CA INDEX NAME)

CM 1

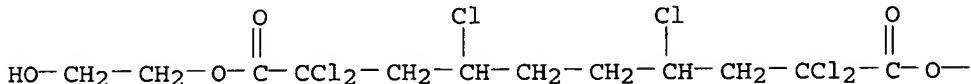
CRN 77304-38-2
CMF C11 H10 Cl2 F8 O6

RN 77363-26-9 HCAPLUS
 CN Decanedioic acid, 2,2,4,7,9,9-hexachloro-, bis(2-hydroxyethyl) ester, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 77363-25-8
CMF C14 H20 Cl6 O6

PAGE 1-A



PAGE 1-B

— CH₂—CH₂—OH

L39 ANSWER 5 OF 5 HCPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1980:185910 HCPLUS
 DOCUMENT NUMBER: 92:185910
 TITLE: Nonimmunogenic polypeptides
 INVENTOR(S): Davis, Frank F.; Van Es, Theodorus; Palczuk, Nicholas C.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S., 12 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4179337	A	19791218	US 1977-819831	19770728
PRIORITY APPLN. INFO.:			US 1973-381191	19730720
			US 1975-596931	19750717

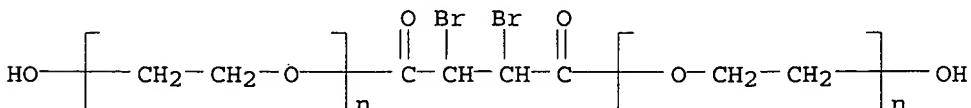
AB Polypeptides such as enzymes or insulin are coupled to polyethylene glycol (PEG) or polypropylene glycol to give a phys. active nonimmunogenic water for polypeptide composition. The glycols protect the peptides from loss of activity and the composition can be injected with no immunogenic response. Thus, PEG 750 [25322-68-3] or PEG 2000 was dissolved in anhydrous C₆H₆ containing Na₂CO₃. The solution was cooled and cyanuric chloride [108-77-0]

was added to give PEG 4-hydroxy-6-chloro-1,3,5-triazine (I) [58914-58-2]. I was added to insulin, dissolved in 0.1 M borate buffer, pH 9.2, to give a PEG-4-hydroxy-1,3,5-triazin-6-yl conjugate (II). II had insulin activity of .apprx.50% of insulin activity when injected into rabbits based on weight of conjugated insulin administered. II also had no antigenic activity visavis insulin antiserum.

IT 73342-27-5P
 RL: PRP (Properties); PREP (Preparation)
 (preparation and conjugation of, with UDP glucuronyl transferase, for nonimmunogenic preps.)

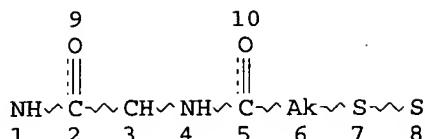
RN 73342-27-5 HCPLUS

CN Poly(oxy-1,2-ethanediyl), α,α' -(2,3-dibromo-1,4-dioxo-1,4-butanediyl)bis[ω -hydroxy- (9CI) (CA INDEX NAME)



=> d que 118

L3 STR



NODE ATTRIBUTES:

CONNECT IS E2 RC AT 6
 DEFAULT MLEVEL IS ATOM
 GGCAT IS LIN LOC SAT AT 6
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

L5	189 SEA FILE=REGISTRY SSS FUL L3
L6	8 SEA FILE=REGISTRY ABB=ON PLU=ON L5 AND PMS/CI
L7	1 SEA FILE=REGISTRY ABB=ON PLU=ON PEG/CN
L8	9851 SEA FILE=REGISTRY ABB=ON PLU=ON 25322-68-3/CRN
L9	9852 SEA FILE=REGISTRY ABB=ON PLU=ON L7 OR L8
L10	4 SEA FILE=HCAPLUS ABB=ON PLU=ON L6
L11	3 SEA FILE=HCAPLUS ABB=ON PLU=ON L5 AND L9
L12	6 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 OR L11
L16	206741 SEA FILE=HCAPLUS ABB=ON PLU=ON POLYOXYALKYLENES+OLD, NT/CT
L17	4 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 AND L5
L18	6 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 OR L17

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L18 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2001:875456 HCAPLUS

DOCUMENT NUMBER: 137:190482

TITLE: Targeted PEG-based bioconjugates enhance the cellular uptake and transport of a HIV-1 TAT nonapeptide
 Ramanathan, Srinivasan; Qiu, Bo; Pooyan, Shahriar;
 Zhang, Guobao; Stein, Stanley; Leibowitz, Michael J.;
 Sinko, Patrick. J.

CORPORATE SOURCE: Rutgers - The State University of New Jersey, College of Pharmacy, Piscataway, NJ, 08854, USA

SOURCE: Journal of Controlled Release (2001), 77(3), 199-212
 CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal.

LANGUAGE: English

AB We previously described the enhanced cell uptake and transport of R.I-K(biotin)-Tat9, a large (.apprx.1500 Da) peptidic inhibitor of HIV-1 Tat protein, via SMVT, the intestinal biotin transporter. The aim of the present study was to investigate the feasibility of targeting biotinylated PEG-based conjugates to SMVT in order to enhance cell uptake and transport of Tat9. The 29 kDa peptide-loaded bioconjugate (PEG:(R.I-Cys-K(biotin)-Tat9)8) used in these studies contained eight copies of R.I-K(biotin)-Tat9 appended to PEG by means of a cysteine linkage. The absorptive transport

of biotin-PEG-3400 (0.6-100 μM) and the bioconjugate (0.1-30 μM) was studied using Caco-2 cell monolayers. Inhibition of biotin-PEG-3400 by pos. controls (biotin, biocytin, and desthiobiotin) was also determined. Uptake of these two compds. was also determined in CHO cells transfected with human SMVT (CHO/hSMVT) and control cells (CHO/pSPORT) over the concentration ranges

of

0.05-12.5 μM and 0.003-30 μM , resp. Nonbiotinylated forms of these two compds., PEG-3350 and PEG:(R.I-Cys-K-Tat9)8, were used in the control studies. Biotin-PEG-3400 transport was found to be concentration-dependent and saturable in Caco-2 cells ($K_m=6.61 \mu\text{M}$) and CHO/hSMVT cells ($K_m=1.26 \mu\text{M}$). Transport/uptake was significantly inhibited by pos. control substrates of SMVT. PEG:(R.I-Cys-K(biotin)Tat9)8 also showed saturable transport kinetics in Caco-2 cells ($K_m=6.13 \mu\text{M}$) and CHO/hSMVT cells ($K_m=8.19 \mu\text{M}$). Maximal uptake in molar equivalents of R.I-Cys-K(biotin)Tat9 was 5.7 times greater using the conjugate vs. the biotinylated peptide alone. Transport of the nonbiotinylated forms was significantly lower ($P<0.001$) in all cases. The present results demonstrate that biotin-PEG-3400 and PEG:(R.I-Cys-K(biotin)Tat9)8 interact with human SMVT to enhance the cellular uptake and transport of these larger mols. and that targeted bioconjugates may have potential for enhancing the cellular uptake and transport of small peptide therapeutic agents.

CC

63-5 (Pharmaceuticals)

Section cross-reference(s): 1

IT

Polyoxyalkylenes, biological studies

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(targeted PEG-based bioconjugates enhance cellular uptake and transport of HIV-1 TAT nonapeptide)

IT

449762-62-3DP, ethoxylated

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(targeted PEG-based bioconjugates enhance cellular uptake and transport of HIV-1 TAT nonapeptide)

IT

25322-68-3, PEG 199869-49-3 449762-61-2

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(targeted PEG-based bioconjugates enhance cellular uptake and transport of HIV-1 TAT nonapeptide)

IT

449762-62-3DP, ethoxylated

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(targeted PEG-based bioconjugates enhance cellular uptake and transport of HIV-1 TAT nonapeptide)

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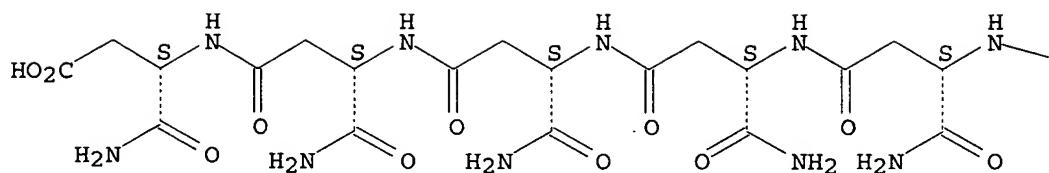
449762-62-3 HCPLUS

CN

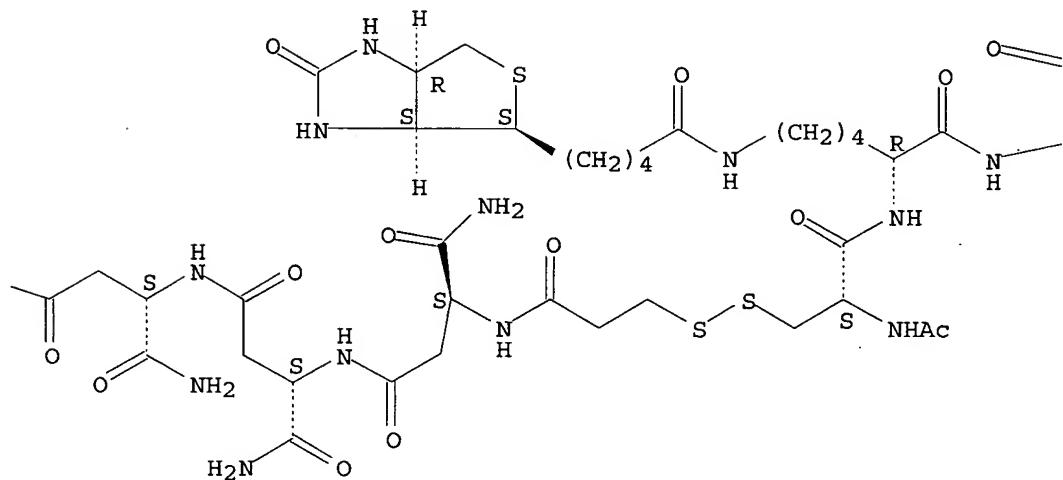
D-Argininamide, N-acetyl-D-cysteinyl-N6-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-D-lysyl-D-arginyl-D-arginyl-D-arginyl-D-glutaminyl-D-arginyl-D-arginyl-D-lysyl-D-lysyl-, (1 \rightarrow 1')-disulfide with N-(3-mercaptop-1-oxopropyl)-L- α -asparaginyl-L- α -asparaginyl-L- α -asparaginyl-L- α -asparaginyl-L- α -asparaginyl-L- α -asparagine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

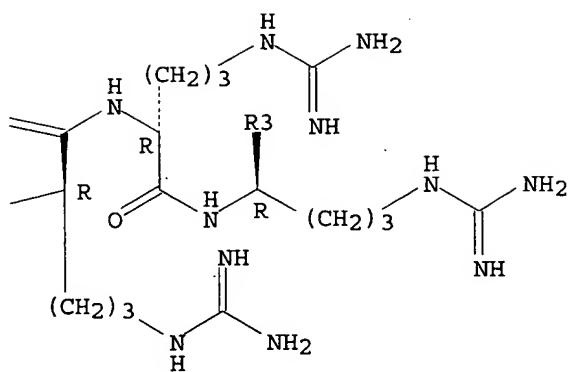
PAGE 1-A



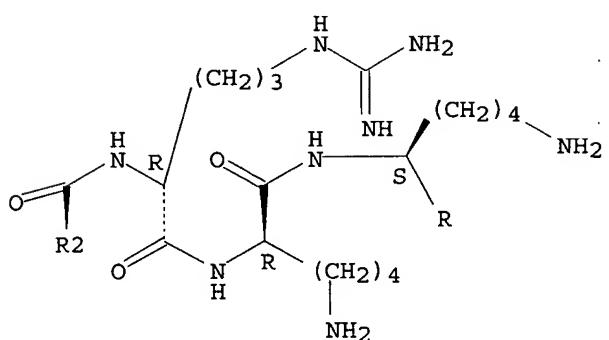
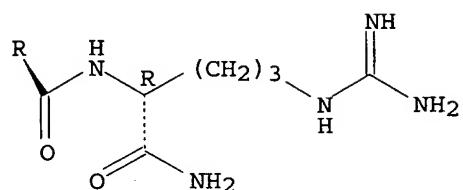
PAGE 1-B



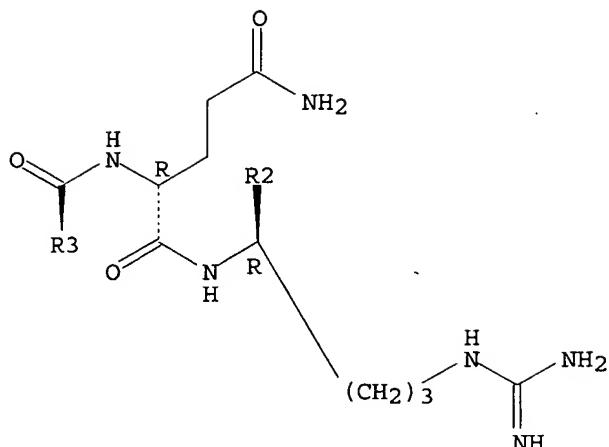
PAGE 1-C



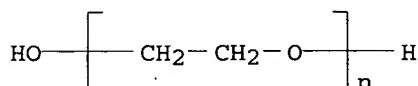
PAGE 2-A



PAGE 3 - A



IT 25322-68-3, PEG
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(targeted PEG-based bioconjugates enhance cellular uptake and transport
of HIV-1 TAT nonapeptide)
RN 25322-68-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α -hydro- ω -hydroxy- (9CI) (CA INDEX
NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:581916 HCAPLUS
DOCUMENT NUMBER: 135:175376
TITLE: Ligand for vascular endothelial growth factor receptor
INVENTOR(S): Tchistiakova, Lioudmila; Li, Shengmin; Pietrzynski,
 Grzegorz; Alakhov, Valery
PATENT ASSIGNEE(S): Supratek Pharma Inc., Can.
SOURCE: PCT Int. Appl., 86 pp.
 CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001057067	A1	20010809	WO 2001-IB135	20010202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,				

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2399022 AA 20010809	CA 2001-2399022	20010202	
US 2002058619 A1 20020516	US 2001-775743	20010202	
US 6733755 B2 20040511			
EP 1252177 A1 20021030	EP 2001-948985	20010202	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003528824 T2 20030930	JP 2001-557898	20010202	
PRIORITY APPLN. INFO.:	US 2000-180568P	P 20000204	
	WO 2001-IB135	W 20010202	

OTHER SOURCE(S): MARPAT 135:175376

AB The present invention relates to compns. comprised of a peptide ligand or derivs. thereof that are capable of specific binding to the high affinity receptor-1 of vascular endothelial growth factor (VEGF) and structure similar receptors. The invention further provides a peptide ligand or derivs. thereof that are capable of inhibiting angiogenesis induced by VEGF. The present invention also provides a method for treatment or diagnosis of disease associated with angiogenesis in a patient in need of therapy comprising administering to the patient an effective amount of the pharmaceutical composition of the present invention and a pharmaceutical acceptable carrier.

IC ICM C07K004-12

ICS C07K007-08; A61K038-03; A61K038-10; C12N015-11

CC 1-8 (Pharmacology)

Section cross-reference(s): 34, 63

IT **Polyoxyalkylenes, reactions**

RL: RCT (Reactant); RACT (Reactant or reagent)

(peptide ligand for vascular endothelial growth factor receptor that inhibit angiogenesis)

IT 9003-99-0DP, Peroxidase, conjugates with VEGF receptor ligand peptides 26247-79-0DP, reaction products with paclitaxel, peptide sequence conjugate derivs. 26658-46-8DP, reaction products with piperidyldithiopropionic acid, peptide sequence conjugate derivs.

106392-12-5DP, amine-terminated derivs., reaction products with pyridyldithiopropionic acid, peptide sequence conjugate derivs.

117527-50-1DP, reaction products with FMOC/succinimidyl-terminated polyethylene glycol and polyglutamic acid, peptide sequence conjugate derivs. 264257-54-7DP, reaction products with paclitaxel succinate, peptide sequence conjugate derivs. 353483-27-9DP, conjugates with peroxidase 353483-28-0DP, conjugates with Leurubicin 353483-31-5P 353483-33-7P 353483-36-0DP, peptide sequence conjugate derivs.

353483-38-2DP, reaction products with amine-terminated polyethylene glycol, peptide sequence conjugate derivs. 353483-40-6DP, conjugates with Paclitaxel succinate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(peptide ligand for vascular endothelial growth factor receptor that inhibit angiogenesis)

IT 9002-98-6 24991-53-5 **25322-68-3**, Polyethylene glycol

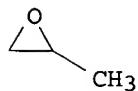
25962-31-6 26247-79-0, Polyglutamic acid sodium salt 33069-62-4, Paclitaxel 68181-17-9, N-Succinimidyl-3-[2-pyridyldithio]propionate 70774-25-3, L-Leucyl-doxorubicin 117527-50-1 264257-54-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(peptide ligand for vascular endothelial growth factor receptor that

IT inhibit angiogenesis)
 IT 353483-36-0P 353483-38-2P 353483-44-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (peptide ligand for vascular endothelial growth factor receptor that inhibit angiogenesis)
 IT 106392-12-5, pluronic F127
 RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 (reactant and formulation with; peptide ligand for vascular endothelial growth factor receptor that inhibit angiogenesis)
 IT 106392-12-5DP, amine-terminated derivs., reaction products with pyridyldithiopropionic acid, peptide sequence conjugate derivs.
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (peptide ligand for vascular endothelial growth factor receptor that inhibit angiogenesis)
 RN 106392-12-5 HCAPLUS
 CN Oxirane, methyl-, polymer with oxirane, block (9CI) (CA INDEX NAME)

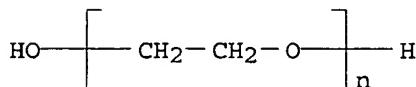
CM 1

CRN 75-56-9
CMF C3 H6 O

CM 2

CRN 75-21-8
CMF C2 H4 O

IT 25322-68-3, Polyethylene glycol
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (peptide ligand for vascular endothelial growth factor receptor that inhibit angiogenesis)
 RN 25322-68-3 HCAPLUS
 CN Poly(oxy-1,2-ethanediyl), α -hydro- ω -hydroxy- (9CI) (CA INDEX NAME)



IT 353483-44-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

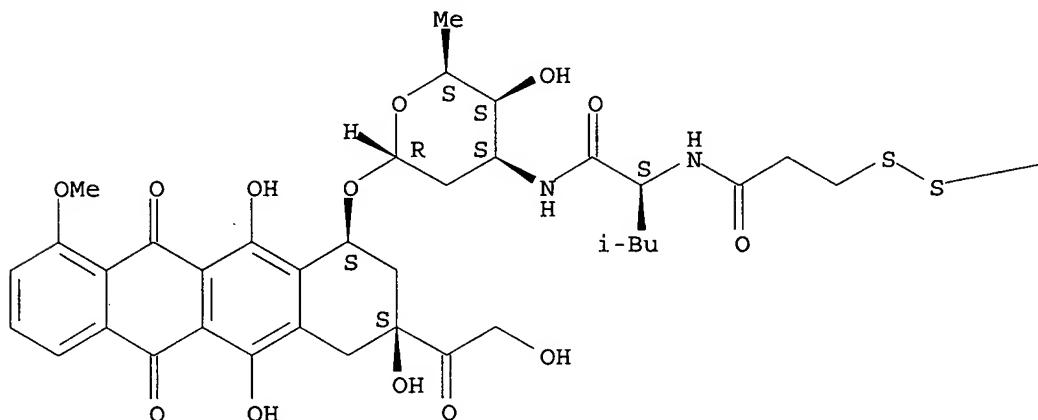
(peptide ligand for vascular endothelial growth factor receptor that inhibit angiogenesis)

RN 353483-44-0 HCAPLUS

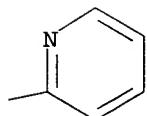
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[(2S)-4-methyl-1-oxo-2-[[1-oxo-3-(2-pyridinylidithio)propyl]amino]pentyl]amino]- α -L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 106392-12-5, pluronic F127

RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(reactant and formulation with; peptide ligand for vascular endothelial growth factor receptor that inhibit angiogenesis)

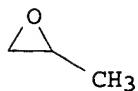
RN 106392-12-5 HCAPLUS

CN Oxirane, methyl-, polymer with oxirane, block (9CI) (CA INDEX NAME)

CM 1

CRN 75-56-9

CMF C3 H6 O



CM 2

CRN 75-21-8
CMF C2 H4 O

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

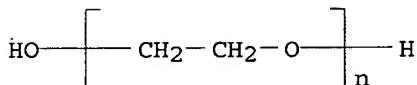
L18 ANSWER 3 OF 6 HCPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2001:12528 HCPLUS
 DOCUMENT NUMBER: 134:91177
 TITLE: Combinations for introducing nucleic acids into cells for gene therapy
 INVENTOR(S): Plank, Christian; Stemberger, Axel; Scherer, Franz
 PATENT ASSIGNEE(S): Germany
 SOURCE: PCT Int. Appl., 105 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000708	A1	20010104	WO 2000-EP5778	20000621
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1063254	A1	20001227	EP 1999-112260	19990625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19956502	A1	20010531	DE 1999-19956502	19991124
CA 2377207	AA	20010104	CA 2000-2377207	20000621
EP 1198489	A1	20020424	EP 2000-936907	20000621
EP 1198489	B1	20040428		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003503370	T2	20030128	JP 2001-506715	20000621
AT 265488	E	20040515	AT 2000-936907	20000621
US 2003026840	A1	20030206	US 2001-23317	20011217
PRIORITY APPLN. INFO.:			EP 1999-112260 A 19990625	
			DE 1999-19956502 A 19991124	
			WO 2000-EP5778 W 20000621	

AB The invention relates to combinations of a carrier and a complex, which consists of a nucleic-acid mol. and a copolymer to be used as drug delivery system in gene therapy. Said copolymer consists of an amphiphilic polymer, preferably polyethylene glycol and a charged effector

mol., in particular, a peptide or peptide derivative. The invention also relates to the use of the combinations for transferring nucleic acid mols. into cells. The carrier is non-biodegradable or biodegradable, e.g. collagen. Copolymer-protected gene vectors were used to transfect cells and also applied as implants.

IC ICM C08G065-329
 ICS C08G065-333; A61K048-00; C12N015-87; A61K047-48
 CC 63-7 (Pharmaceuticals)
 IT **Polyoxalkylenes, reactions**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (derivs.; combinations for introducing nucleic acids into cells for gene therapy)
 IT 60-32-2 107-96-0, 3-Mercaptopropionic acid 2127-03-9 16874-06-9,
 L-Glutamic acid di-tert-butylerster 25322-68-3D, Polyethylene
 glycol, derivs. 185462-59-3 316381-66-5 316381-67-6 316381-68-7
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (combinations for introducing nucleic acids into cells for gene therapy)
 IT 68617-64-1P 185462-59-3DP, conjugate with copolymer via disulfide bond
 296787-33-2P 316381-65-4P 316381-69-8P 316381-71-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (combinations for introducing nucleic acids into cells for gene therapy)
 IT 25322-68-3D, Polyethylene glycol, derivs.
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (combinations for introducing nucleic acids into cells for gene therapy)
 RN 25322-68-3 HCPLUS
 CN Poly(oxy-1,2-ethanediyl), α -hydro- ω -hydroxy- (9CI) (CA INDEX NAME)

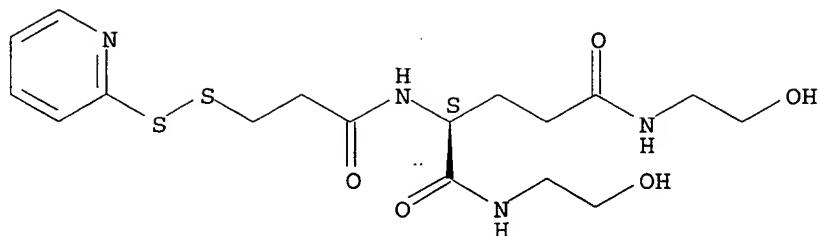


IT 316381-65-4P 316381-71-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (combinations for introducing nucleic acids into cells for gene therapy)
 RN 316381-65-4 HCPLUS
 CN Pentanediamide, N,N'-bis(2-hydroxyethyl)-2-[[1-oxo-3-(2-pyridinyl)dithio)propyl]amino]-, (2S)-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 316381-64-3
 CMF C17 H26 N4 O5 S2

Absolute stereochemistry.



RN 316381-71-2 HCPLUS

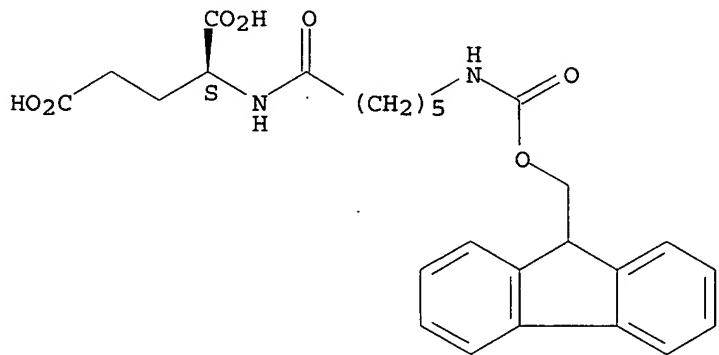
CN L-Glutamic acid, N-[6-[[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-1-oxohexyl]-, polymer with (2S)-N,N'-bis(2-hydroxyethyl)-2-[[1-oxo-3-(2-pyridinyl)dithio)propyl]amino]pentanediamide (9CI) (CA INDEX NAME)

CM 1

CRN 316381-69-8

CMF C26 H30 N2 O7

Absolute stereochemistry.

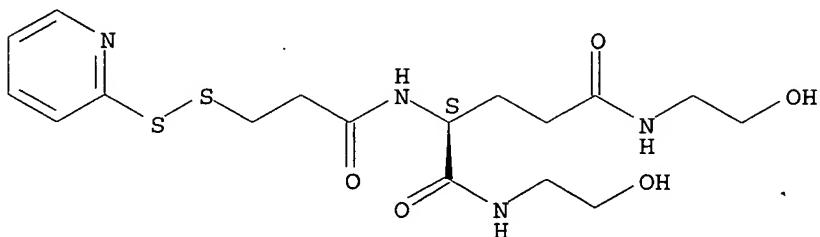


CM 2

CRN 316381-64-3

CMF C17 H26 N4 O5 S2

Absolute stereochemistry.



REFERENCE COUNT:

7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 6 HCPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2000:911282 HCPLUS
 DOCUMENT NUMBER: 134:71899
 TITLE: Preparation of functional poly- α -amino acid derivatives useful for the modification of biologically active materials
 INVENTOR(S): Schacht, Etienne Honore; Toncheva, Veska
 PATENT ASSIGNEE(S): Universiteit Gent, Belg.
 SOURCE: PCT Int. Appl., 65 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078791	A2	20001228	WO 2000-BE66	20000619
WO 2000078791	A3	20011213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2377267	AA	20001228	CA 2000-2377267	20000619
EP 1189971	A2	20020327	EP 2000-938349	20000619
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			EP 1999-870125	A 19990617
			WO 2000-BE66	W 20000619

AB Linear poly- α -amino-acid derivs. having at least glutamic, aspartic or serinic repeating units and addnl. a functional group (other than alc.) at one or both ends of the polymer backbone and/or only a single functional group as a side group on the polymer backbone were prepared for use in the modification of biol. active materials. Thus, poly[N-(2-hydroxyethyl)-L-glutamine] (PHEG) was prepared by polymerization of γ -trichloroethyl-L-glutamate in the presence of Ph₃CNHCH₂CH₂NH₂, aminolysis with ethanolamine, and deprotection. Enzymic degradation of PHEG is shown in a graph.

IC ICM C07K001-00

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 35, 63

IT 26690-80-2P 27878-59-7DP, amide-terminated and N-acyl protected

92739-24-7DP, amide-terminated and N-acyl protected 314295-31-3P

314295-32-4P 314295-33-5P 314295-34-6P 314295-39-1DP,

amide-terminated and N-acyl protected 314295-40-4P 314295-42-6P

314295-43-7P 314295-44-8P 314295-45-9P 314295-46-0P 314295-47-1P

314295-48-2P 314295-49-3P 314295-50-6P

314295-51-7P 314295-52-8P 314295-54-0P 314295-55-1P

314295-57-3P 314295-58-4P 314295-59-5P 314295-60-8P

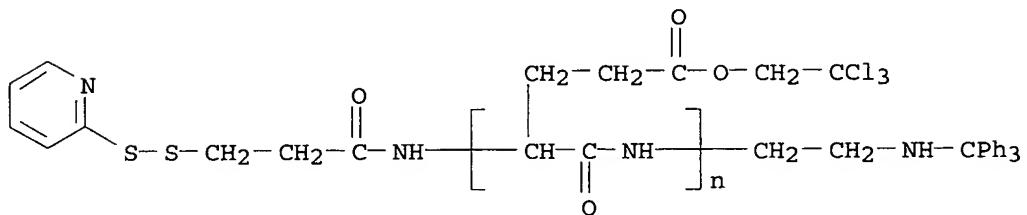
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);

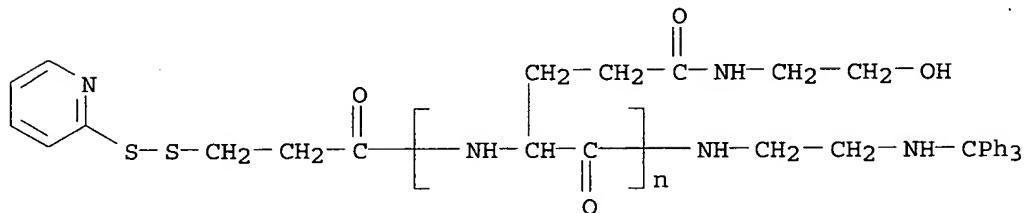
USES (Uses)

(preparation of functional poly- α -amino acid derivs. useful for the

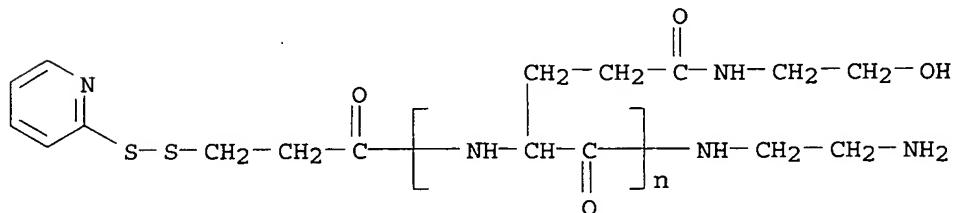
modification of biol. active materials)
 IT 314295-49-3P 314295-50-6P 314295-51-7P
314295-52-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
 USES (Uses)
 (preparation of functional poly- α -amino acid derivs. useful for the
 modification of biol. active materials)
 RN 314295-49-3 HCAPLUS
 CN Poly[imino[(2S)-1-oxo-2-[3-oxo-3-(2,2,2-trichloroethoxy)propyl]-1,2-
 ethanediyl], α -[2-[(triphenylmethyl)aminoethyl]- ω -[1-oxo-3-
 (2-pyridinyldithio)propyl]amino]- (9CI) (CA INDEX NAME)



RN 314295-50-6 HCAPLUS
 CN Poly[imino[(1S)-1-[3-[(2-hydroxyethyl)amino]-3-oxopropyl]-2-oxo-1,2-
 ethanediyl], α -[1-oxo-3-(2-pyridinyldithio)propyl]- ω -[(2-
 [(triphenylmethyl)amino]ethyl]amino]- (9CI) (CA INDEX NAME)

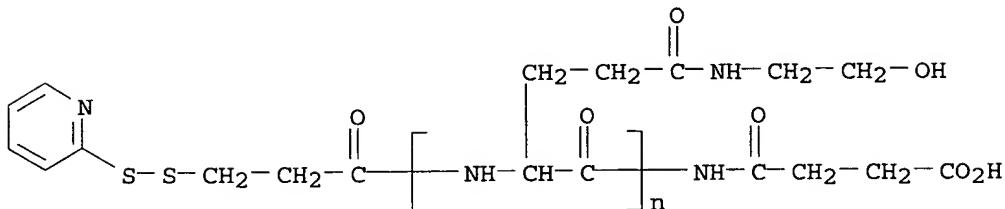


RN 314295-51-7 HCAPLUS
 CN Poly[imino[(1S)-1-[3-[(2-hydroxyethyl)amino]-3-oxopropyl]-2-oxo-1,2-
 ethanediyl], α -[1-oxo-3-(2-pyridinyldithio)propyl]- ω -[(2-
 aminoethyl)amino]- (9CI) (CA INDEX NAME)



RN 314295-52-8 HCAPLUS
 CN Poly[imino[(1S)-1-[3-[(2-hydroxyethyl)amino]-3-oxopropyl]-2-oxo-1,2-
 ethanediyl], α -[1-oxo-3-(2-pyridinyldithio)propyl]- ω -[(3-

carboxy-1-oxopropyl)amino]- (9CI) (CA INDEX NAME)



L18 ANSWER 5 OF 6 HCPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:299367 HCPLUS

DOCUMENT NUMBER: 129:58748

TITLE: A novel method for surface modification to promote cell attachment to hydrophobic substrates

AUTHOR(S): Neff, J. A.; Caldwell, K. D.; Tresco, P. A.

CORPORATE SOURCE: Center for Biopolymers at Interfaces, Department of Bioengineering, University of Utah, Salt Lake City, UT, 84112, USA

SOURCE: Journal of Biomedical Materials Research (1998), 40(4), 511-519

CODEN: JBMRBG; ISSN: 0021-9304

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The ability to study and regulate cell behavior at a biomaterial interface requires strict control over material surface chemical. Perhaps the greatest challenge to researchers working in this area is preventing the fouling of a given surface due to uncontrolled protein adsorption. This work describes a method for coupling peptides to hydrophobic materials for the purpose of simultaneously preventing nonspecific protein adsorption and controlling cell adhesion. A hexapeptide containing the ubiquitous RGD cell-adhesion motif was coupled to polystyrene (PS) via a polyethylene oxide (PEO) tether in the form of a modified PEO/PPO/PEO triblock copolymer. Triblocks were adsorbed onto PS at a d. of $3.3 \pm (5.14 \times 10^{-4})$ mg/m² ($1.4 \times 10^5 \pm 2.12 \times 10^1$ mols./μm²), which was determined by isotope ¹²⁵I labeling. The peptide, GRGDSY, was activated at the N terminus with N-Succinimidyl 3-(2-pyridyldithio) propionate and coupled to immobilized tri-blocks where the terminal hydroxyls had been converted to sulfhydryl groups. Surface peptide d. was measured by amino acid anal. and found to be $1.4 \times 10^4 \pm 0.47 \times 10^4$ mols./μm². PS modified with PEO/PPO/PEO copolymers alone was found to be inert to cell adhesion both in the presence of serum proteins and when exposed to activated RGD peptide. In contrast, PS conjugated with RGD via end-group-activated PEO/PPO/PEO copolymers supported cell adhesion and spreading. The surface coupling scheme reported here should prove valuable for studying cell-ligand interactions under simplified and highly controlled conditions.

CC 63-7 (Pharmaceuticals)

Section cross-reference(s): 34

IT 7693-46-1, p-Nitrophenyl chloroformate 106139-15-5 106392-12-5
, Pluronic F108 140457-22-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(novel method for surface modification to promote cell attachment to hydrophobic substrates)

IT 68181-17-9P 208331-36-6P 208539-80-4P 208539-81-5P
 208539-82-6P 208539-83-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (novel method for surface modification to promote cell attachment to hydrophobic substrates)

IT 106392-12-5, Pluronic F108
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (novel method for surface modification to promote cell attachment to hydrophobic substrates)

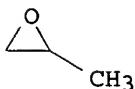
RN 106392-12-5 HCAPLUS

CN Oxirane, methyl-, polymer with oxirane, block (9CI) (CA INDEX NAME)

CM 1

CRN 75-56-9

CMF C3 H6 O



CM 2

CRN 75-21-8

CMF C2 H4 O



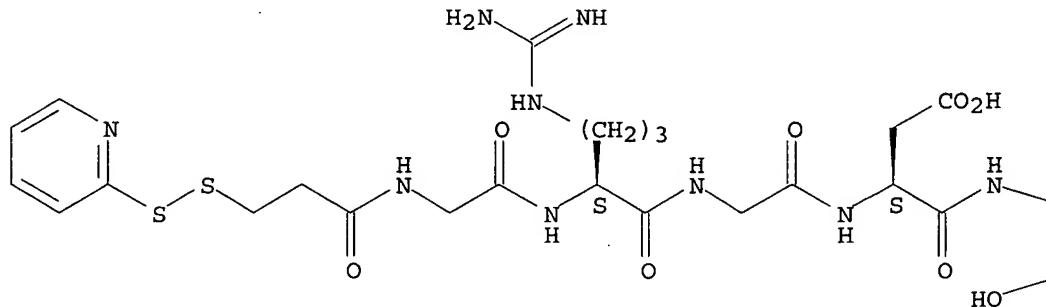
IT 208331-36-6P 208539-83-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (novel method for surface modification to promote cell attachment to hydrophobic substrates)

RN 208331-36-6 HCAPLUS

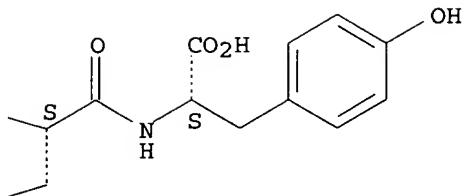
CN L-Tyrosine, N-[1-oxo-3-(2-pyridinyldithio)propyl]glycyl-L-arginylglycyl-L- α -aspartyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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PAGE 1-B



RN 208539-83-7 HCAPLUS

CN Oxirane, methyl-, polymer with oxirane, 1-ester with N-[3-[(2-carboxyamino)ethyl]dithio]-1-oxopropylglycyl-L-arginylglycyl-L- α -aspartyl-L-seryl-L-tyrosine (9CI) (CA INDEX NAME)

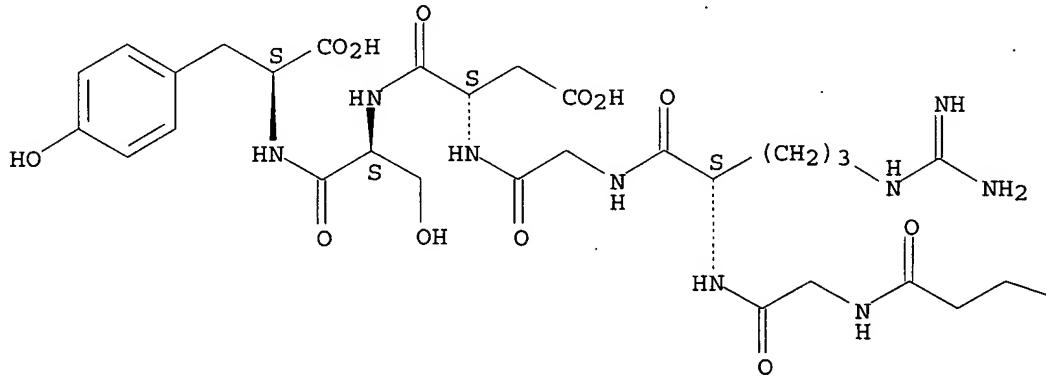
CM 1

CRN 208342-27-2

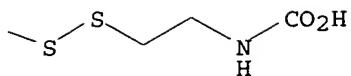
CMF C32 H48 N10 O14 S2

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

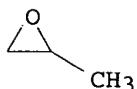


CM 2

CRN 9003-11-6
 CMF (C3 H6 O . C2 H4 O)x
 CCI PMS

CM 3

CRN 75-56-9
 CMF C3 H6 O



CM 4

CRN 75-21-8
 CMF C2 H4 O



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 6 HCPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1997:504550 HCPLUS
 DOCUMENT NUMBER: 127:205848
 TITLE: Pegylated peptides. V. Carboxy-terminal PEGylated analogs of growth hormone-releasing factor (GRF) display enhanced duration of biological activity in vivo
 AUTHOR(S): Campbell, R. M.; Heimer, E. P.; Ahmad, M.; Eisenbeis, H. G.; Lambros, T. J.; Lee, Y.; Miller, R. W.; Stricker, P. R.; Felix, A. M.
 CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc., Nutley,

SOURCE: NJ, USA
 Journal of Peptide Research (1997), 49(6), 527-537
 CODEN: JPERFA; ISSN: 1397-002X

PUBLISHER: Munksgaard
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB In the present study, human growth hormone-releasing factor (hGRF) and analogs were successfully pegylated at the carboxy-terminus using a novel solid- and solution-phase strategy. Following synthesis, these pegylated hGRF analogs were evaluated for in vitro and in vivo biol. activity. Specifically, hGRF(1-29)-NH₂, [Ala15]-hGRF(1-29)-NH₂, [des-NH₂-Tyr₁,D-Ala₂,Ala15]-hGRF(1-29)-NH₂ and [His₁,Val₂,Gln₈,Ala₁₅,Leu₂₇]-hGRF(1-32)-OH were each C-terminally extended using a Gly-Gly-Cys-NH₂ spacer (previously demonstrated not to alter intrinsic biol. activity), and then monopegylated via coupling to an activated dithiopyridyl-PEG reagent. PEG moieties of 750, 2000, 5000 or 10,000 mol. weight (MW) were examined to determine

the effect of polymer weight on activity. Initial biol. evaluations in vitro revealed that all C-terminally pegylated hGRF analogs retained high growth hormone (GH)-releasing potencies, regardless of the MW of PEG polymer employed. Two of these pegylated hGRF analogs, [des-NH₂-Tyr₁,D-Ala₂,Ala15]-hGRF(1-29)-Gly-Gly-Cys(NH₂)-S-Nle-PEG5000 and [His₁,Val₂,Gln₈,Ala₁₅,Leu₂₇]-hGRF(1-32)-Gly-Cys(NH₂)-S-Nle-PEG5000, were subsequently evaluated in both pig and mouse models and found to be highly potent (in vivo potency range = 12-55-fold that of native hGRF). Relative to their non-pegylated counterparts, these two pegylated hGRF analogs exhibited enhanced duration of activity.

CC 34-3 (Amino Acids, Peptides, and Proteins)
 Section cross-reference(s): 2

IT 88504-13-6P 144281-21-0P 144281-22-1P 158598-85-7P

194535-63-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and enhanced activity duration of carboxy-terminal poly(ethylene glycol) growth hormone-releasing factor analogs)

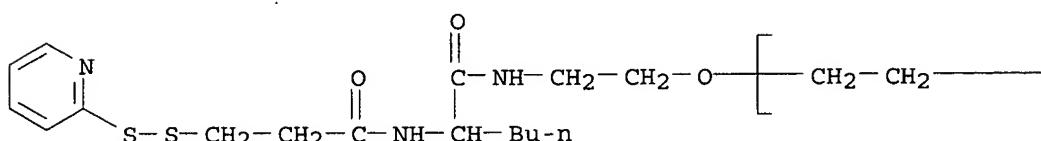
IT 194535-63-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and enhanced activity duration of carboxy-terminal poly(ethylene glycol) growth hormone-releasing factor analogs)

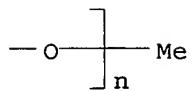
RN 194535-63-2 HCPLUS

CN Poly(oxy-1,2-ethanediyl), α-methyl-ω-[2-[[1-oxo-2-[[1-oxo-3-(2-pyridinyldithio)propyl]amino]hexyl]amino]ethoxy]-, (S)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT